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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MARK A. HOFFMAN and DAVID P. MCCALLIE JR

Appeal 2008-0474
Application 09/981,248
Technology Center 1600

Decided: August 28, 2008

Before TONI R. SCHEINER, HOWARD B. BLANKENSHIP, and ERIC GRIMES, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method and system for predicting a patient's response to drugs. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm and enter a new ground of rejection.

BACKGROUND

"Scientists have uncovered and continue to uncover a number of correlations between drug responses (or phenotypes) and the specific genetic makeup (or genotype) of a patient. Many variations in genotype have been clearly associated with variable responses to drugs." (Specification 2.) "Information about the individual's genetic deviation from a typical genetic trait can be predictive of whether or not the drug will be either toxic or inefficient at the recommended dosage. This information should be considered to avoid adverse, or other atypical, reactions." (*Id.* at 3.)

DISCUSSION

1. CLAIMS

Claims 25-30, 55-60, and 85-91 are pending and on appeal. The claims subject to each rejection have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). We will focus on claims 25 and 28. Claims 25-28 read as follows:

> 25. A method in a computer system for processing hereditary data related to the use of clinical agents by a person, comprising the steps of:
>
> receiving a genetic test result value for the person;
>
> querying a computerized table listing polymorphism values and atypical clinical events associated with the polymorphism values;
>
> determining if the genetic test result value is a polymorphism value associated with an atypical clinical event, and if so, accessing a list of risk-associated agents; and
>
> outputting an interpretation of the genetic test result value and the list of risk-associated agents.

26. The method of claim 25, further comprising the step of determining if the person has been exposed to an agent on the list of risk-associated agents.

27. The method of claim 26, wherein the step of determining if the person has been exposed includes accessing an electronic medical record of the person.

28. The method of claim 27, wherein the electronic medical record is stored within a comprehensive healthcare system.

2. OBVIOUSNESS I

Claims 25-27, 29, 30, 55-57, 59, 60, 85-87, and 89-91 stand rejected under 35 U.S.C. § 103 as obvious in view of Ichikawa,[1] Evans,[2] and Reinhoff.[3] The Examiner finds that Ichikawa teaches a method of determining a drug dosage based on genetic testing that shows a polymorphism associated with atypical clinical events on administration of certain drugs (Answer 4). The Examiner finds that Evans teaches a computerized table showing atypical clinical events associated with different polymorphisms (*id.*) and "automated systems to associate an individual's genotype with polymorphic genes in order to optimize drug administration and disease treatment" (*id.* at 5). The Examiner finds that Reinhoff teaches populating a computerized database with genotypic and phenotypic data,

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[1] Ichikawa, "Single nucleotide polymorphism to disclose severe side-effects or proper dosage for each patient," *Internal Medicine*, Vol. 39, pp. 523-524 (2000).
[2] Evans et al., "Pharmacogenomics: Translating functional genomics into rational therapeutics," *Science*, Vol. 286, pp. 487-491 (1999).
[3] Reinhoff, Jr. et al., US 2002/0049772 A1, published April 25, 2002.

including data associated with response to drugs, and analyzing the data in the database (*id.*).

The Examiner concludes that it would have been obvious to computerize the genetic screening method of Ichikawa, as taught by Reinhoff, and access a computerized list of treatment options, as taught by Evans, in order to identify the appropriate treatment and dosage for individual patients (*id.* at 5-6).

We agree with the Examiner that the cited references support a prima facie case of obviousness. Ichikawa teaches that people with certain mutations in the thiopurine S-methyltransferase (TPMT) gene do not efficiently metabolize drugs such as azathioprine, such that the normal dosage of azathioprine causes "severe hematopoietic toxicity" (Ichikawa, page 523, left-hand column). Ichikawa teaches that toxicity can be avoided by decreasing the dose by 50% for patients who have a heterozygous mutation and by decreasing the dose by 8-15 fold for patients with homozygous mutations (*id.*). Ichikawa concludes that "[a]s shown in this paper, we may be able to know beforehand from the information of genetic polymorphism, whether a patient will respond or show adverse effects, and may know further the proper dosage for each patient" (*id.* at 523, right-hand column).

Evans teaches that genetic polymorphisms in different proteins have been linked to differences between individuals in the efficacy and toxicity of many medications (Evans, abstract). Evans lists several examples of genes having polymorphisms that were known to cause adverse drug effects (*id.* at

489, Table 1). Evans states that a "comprehensive listing is available" at a specific internet web address (*id.*).

Evans also teaches that studies of these differences provide a basis for optimizing drug therapy on the basis of a patient's genetic makeup (*id.*, abstract). Evans states that "automated systems are being developed to determine an individual's genotype for polymorphic genes that are known to be involved . . . in the metabolism and disposition of medications" (*id.* at 490-491). Evans teaches that "[s]uch diagnostics . . . can then become the blueprint for individualizing drug therapy" (*id.* at 491).

Reinhoff discloses a "computer program product that is capable of generating a polymorphic profile for an individual and thereafter, separating individuals based upon their polymorphic profile" (Reinhoff, ¶ 0009). Reinhoff teaches that the computer program product "includes code that compares an individual's polymorphic profile with a plurality of polymorphic profiles. . . . The genetic profiles are stored in a database and the information can be used to gauge drug responses" (*id.* at ¶ 0012). Reinhoff also teaches that the disclosed computer program product "can be used in pharmacogenomics, wherein an individual nucleic acid variation can be used to ascertain whether the efficacy of a pharmaceutical will be amplified or reduced" (*id.* at ¶ 0014).

We agree with the Examiner that the method of claim 25 would have been obvious to a person of ordinary skill in the art based on the cited references. Specifically, Reinhoff teaches a computerized method of comparing a person's polymorphic profile (i.e., genetic test result value) to genetic profiles stored in a database, and identifying the presence of

polymorphisms that indicate whether the person's response to a drug will be amplified or reduced. Evans and Ichikawa teach that there were numerous examples known in the art of polymorphisms that affected patients' responses to specific drugs.

It would have been obvious to a person of ordinary skill in the art to apply the method taught by Reinhoff to identifying polymorphisms known to affect responses to different drugs, because each of Ichikawa, Evans, and Reinhoff teach that drug dosages should be adjusted depending on the polymorphisms that are present in a patient's DNA. See Ichikawa, page 523 ("[W]e may know beforehand from the information of genetic polymorphism . . . the proper dosage for each patient."); Evans, 490("[T]echnology will soon make it feasible to use molecular diagnostics to more precisely select medications and dosages that are optimal for individual patients."); and Reinhoff, ¶ 0056 ("[I]t is . . . possible to allocate different doses to different patient[s] depending on their polymorphic profile.").

Appellants argue that "[t]he Examiner has not located or pointed to any suggestion in the art to combine the three references in the manner suggested by the Examiner" (Appeal Br. 7). Appellants argue that Reinhoff relates to "allocat[ing] the most appropriate dose to subjects enrolled in a treatment study such as a clinical trial" and "submit that one or skill in the art would not use the Reinhoff reference as a motivation to computerize or automate accessing a list of risk-associated agents and outputting the list of risk-associated agents because the treatment is already known" (*id.* at 8-9). That is, "[a]s the treatment to be used in clinical trials as discussed in the

Reinhoff reference is already known, there is no need to access a list of risk-associated agents and output the list of risk-associated agents" (*id.* at 9).

This argument is unpersuasive. Although Reinhoff focuses on using polymorphism analysis in the context of clinical trials of pharmaceuticals, it also states that the disclosed computer program product can be used more generally to "ascertain whether the efficacy of a pharmaceutical will be amplified or reduced" (Reinhoff, ¶ 0014). Taken together with the teachings of Ichikawa and Evans, Reinhoff would have suggested the instantly claimed method to those of ordinary skill in the art.

In addition, Appellants have pointed to no basis on which to conclude that the "list of risk-associated agents" recited in claim 25 must include multiple agents. Thus, claim 25 reads on a method that outputs a list of "risk-associated agents" that consists of only one agent, or even no agents at all if none of the appropriate polymorphisms are found in the genetic test results.

Appellants also argue that the "references, alone or in combination, fail to teach or suggest all the claim features" (Appeal Br. 10). Appellants then go on to discuss why each reference purportedly does not disclose all the claim limitations (see *id.* at 10-13).

Appellants fail to explain, however, why the disclosures of the cited references *considered collectively* do not teach or would not have suggested each of the limitations of the claims on appeal. *See In re Young*, 927 F.2d 588, 591 (Fed. Cir. 1991)("The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art."); *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986)("Non-

obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references."). Appellants' argument is therefore unpersuasive.

We affirm the rejection of claim 25 as obvious in view of Ichikawa, Evans, and Reinhoff. Claims 26, 27, 29, 30, 55-57, 59, 60, 85-87, and 89-91 fall with claim 25 because they were not argued separately.[4] 37 C.F.R. § 41.37(c)(1)(vii).

3. OBVIOUSNESS II

Claims 28, 58, and 88 stand rejected under 35 U.S.C. § 103 as obvious in view of Ichikawa, Evans, Reinhoff, and Fey.[5] The Examiner relies on Ichikawa, Evans, and Reinhoff for the teachings discussed above, and finds that Fey teaches "an electronic database for comprehensive/centralized health care management wherein the databases comprise a plurality of clinical information and test results for individuals" (Answer 6).

The Examiner concludes that it would have been obvious to have accessed the medical records in the method suggested by Ichikawa, Evans, and Reinhoff in a comprehensive healthcare system/database, as taught by Fey, in order to associate a patient's genotypic and phenotypic information in a clinical setting to provide better treatment (*id.* at 7).

We agree with the Examiner's reasoning and conclusion.

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[4] Appellants state that each of Ichikawa, Evans, and Reinhoff does not teach or suggest all of the limitations of independent claims 25, 55, 85, and 91 (Appeal Br. 10-12). Appellants' arguments, however, merely point out the limitations of claims 25, 55, 85, and 91. "A statement which merely points out what a claim recites will not be considered an argument for separate patentability of the claim." 37 C.F.R. § 41.37(c)(1)(vii).

[5] Fey et al., US 2002/0038227 A1, published March 28, 2002.

Appellants do not dispute that Fey would have suggested the limitations that claim 28 adds to claim 25 (see Appeal Br. 13-16). Appellants argue instead that Ichikawa, Evans, and Reinhoff do not teach or suggest all the claim limitations, and "[t]he Fey reference also fails to teach or suggest all of the limitations of [the] independent claims" (Appeal Br. 14). Again, however, the test under § 103 is not whether a specific reference would have suggested all of the limitations of a claimed invention, but what would have been suggested by the cited references considered as a whole. *See In re Young*, 927 F.2d at 591. Appellants' argument is therefore unpersuasive.

Appellants also argue that the references do not support a prima facie case of obviousness because a person of ordinary skill in the art would not have been motivated to combine Ichikawa, Evans, and Reinhoff (Appeal Br. 15-16). This argument is addressed above.

We affirm the rejection of claim 28 as obvious in view of Ichikawa, Evans, Reinhoff, and Fey. Claims 58 and 88 fall with claim 28 because they were not argued separately. 37 C.F.R. § 41.37(c)(1)(vii).

NEW GROUND OF REJECTION

Under the provisions of 37 C.F.R. § 41.50(b), we enter the following new ground of rejection: Claims 85-90 are rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter.

Claims 85-90 are directed to a "computer-readable medium." Appellants' Specification (at 8) defines such a medium as including, among other things, "data in a modulated data signal, such as a carrier wave." A carrier wave or signal is not statutory subject matter because it does not fall

within any of the four categories of statutory subject matter. *See In re Nuijten,* 500 F.3d 1346, 1357 (Fed. Cir. 2007). We thus reject the claims as embracing non-statutory subject matter.

CONCLUSION

The rejection of claims 25-30, 55-60, and 85-91 under 35 U.S.C. § 103(a) is affirmed.

A new rejection of claims 85-90 under 35 U.S.C. § 101 as being directed to non-statutory subject matter is set forth herein. With respect to the affirmed rejection(s), 37 C.F.R. § 41.52(a)(1) provides that "Appellant may file a single request for rehearing within two months of the date of the original decision of the Board."

In addition to affirming the Examiner's rejection(s) of one or more claims, this decision contains a new ground of rejection pursuant to 37 C.F.R. § 41.50(b). 37 C.F.R. § 41.50(b) provides that "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 C.F.R. § 41.50(b) also provides that Appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

Should Appellants elect to prosecute further before the Examiner pursuant to 37 C.F.R. § 41.50(b)(1), in order to preserve the right to seek review under 35 U.S.C. §§ 141 or 145 with respect to the affirmed rejection, the effective date of the affirmance is deferred until conclusion of the prosecution before the Examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If Appellants elect prosecution before the Examiner and this does not result in allowance of the application, abandonment or a second appeal, this case should be returned to the Board of Patent Appeals and Interferences for final action on the affirmed rejection, including any timely request for rehearing thereof.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED, 37 C.F.R § 41.50(b)

dm

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